UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,771	04/07/2005	Louis Casteilla	SERVIER 450 PCT	4717

25666 7590 07/10/2008

THE FIRM OF HUESCHEN AND SAGE
SEVENTH FLOOR, KALAMAZOO BUILDING
107 WEST MICHIGAN AVENUE
KALAMAZOO, MI 49007

EXAMINER	
RAO, SAVITHA M	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
07/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,771	CASTEILLA ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-44* is/are pending in the application.

4a) Of the above claim(s) *33-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/07/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 26-44 are pending and are subject of this office action. Receipt is acknowledged of preliminary amendment filled on 04/07/2005 where claims 1-25 were cancelled and new claims 26-44 were added.

Claims 26-32 is under consideration in the instant office action. Claims 33-44 are withdrawn as being drawn towards non-elected invention.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 04/07/2005. The Examiner has considered the reference cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449. The "International search report" and "international preliminary examination report:" cited on 1449 dated 04/07/2005 has been lined out because it is not a published document and therefore cannot have a date of publication which is required for a citation in the non-patent document area of 1449.

Election/Restrictions

Applicant's election with traverse of Group 1 (claims 26-32) in the reply filed on 06/16/2008 is acknowledged. The traversal is on the ground(s) that a the Hayward, et al. reference used to break the unity in the restriction/election requirement sent on 05/05/2008 does not disclose a composition comprising an antioxidant agent and a mixed PPAR ligand or disclose a composition comprising an antioxidant agent and a

PPARα ligand and a PPARγ ligand, Examiner disagrees with the Applicant and finds the argument unpersuasive.

Examiner would first like to point to paragraph [0002] where the reference teaches that the peroxisome proliferator receptor (PPAR) agonists in the inventions are in particular PPAR α agonists. Furthermore Hayward et al, does indeed discloses a pharmaceutical compositions comprising; a therapeutically effective amount of a composition comprising the first compound being a formula 1 claimed in claim 1 and a second compound which among other compounds includes an antioxidant compound (claim 39). Hence, Examiner maintains that no special technical feature exists between the two inventions and thereby lacks unity of invention.

Thereby the restriction requirement is still deemed proper and is therefore made FINAL.

Claims 33-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed 06/16/2008

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27-30 recites the limitation the "Composition of claim 26". There is insufficient antecedent basis for this limitation in the claim 26 which is drawn towards a combination comprising a combination. It would be remedial to amend the claims to provide a clear antecedent basis for the term "composition".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al (WO 02/34259).

Instant claims 26-32 are drawn to a combination of an antioxidant agent and a mixed PPAR ligand for α and γ receptor sub-types, or a selective PPAR ligand for the receptor subtype and a selective PPAR ligand for the γ receptor sub-type. Further limitations includes, wherein the PPAR ligand is a mixed ligand, wherein the composition comprises an antioxidant, agent, and a selective PPAR ligand for the α an a selective PPAR ligand for the γ receptor sub-type, where in the PPAR ligand for the γ receptor sub-type is rosiglitazone, wherein the composition is a combination of rosiglitazone and coenzyme Q_{10} and a pharmaceutical compositions of the combination with one or more pharmaceutically-acceptable excepients.

Watts disclose a composition comprising a peroxisome proliferator activated receptor (PPAR) activator and a benzoquinone (abstract and page 3, lines 6-8, Claim 1). Watts disclose that the PPAR activator preferred is a fibrate or a thiazolidinedione, more preferably fenofibrate (page 4, lines 14-17). In claim 10, page 26, Watts recites that the PPAR activator in his composition of his claim 1 to be either PPARα or PPARγ.

Furthermore, Watts teaches that PPAR activators are activators of PPARα or PPARγ and a number of activators are known in the art including the fibrate and thiazolidinedione classes of drugs, for which fenofibrate and rosiglitazone respectively are well known examples. Watts additionally teaches that activation of PPARα leads to lowering of serum triglycerides and that fibrates mainly activates PPARα, but bezafibrate has been shown to activate both PPARα and PPARγ (page 6, line 29 to page 7, line 5).). Watts teaches that the preferred benzoquinone or precursor thereof is a ubiquinone or precursor thereof, more preferably, coenzyme Q_{10} or a precursor thereof (page 4, line11-12, claim 4) and teaches that Benzoquinones used in his present invention should have antioxidant properties, such as the ability to scavenge active oxygen species (page 10, lines 11-13). Watts additionally teaches that *in vivo* the oxidized CoQ_{10} is converted to reduced $CoQ_{10}H_2$ or ubiquinal-10, a potent antioxidant in Plasma, in lipoproteins and in tissues (col. 11, lines 27-30). Finally, Watts teaches that his invention also provides a pharmaceutical composition comprising a composition of the invention together with a pharmaceutically acceptable carrier or diluent (col.4, lines 22-24, claim 8).

It is prima facie obvious to one of ordinary skill in the art to substitute benfibrate (Mixed PPARα and PPARγ ligand) instead of fenofibrate (specific PPARα ligand) or rosiglitazone (specific PPARγ ligand) with fenofibrate (specific PPARα ligand) in combination with an antioxidant such as coenzyme Q_{10} taught by Watts et al. Including more than one PPAR ligand, such as one specific to PPARα and another specific to PPARγ in combination with an antioxidant would be well within the capabilities of an

ordinarily skilled artisan. An ordinary skilled artisan would have been motivated to formulate such a composition comprising a combination of an antioxidant and PPAR ligand (mixed ligand or PPARα selective and PPARγ selective ligand) since a combination of PPAR ligand with an antioxidant has been previously taught in the art to be used for lowering triglycerides. Additionally, as taught by Watt's et al, different PPAR activators are known to exert similar physiological action with respect to lowering triglyceride level and substitution of one to another or inclusion of two such agents in a composition would be expected to elicit similar if not additive/synergistic effect. Accordingly, one of ordinary skill in the art would have been imbued with a reasonable expectation of success based on the prior art that a composition comprising PPAR ligand and antioxidant for lowering cholesterol and triglycerides to develop a more effective treatment option for conditions such as obesity and arthrosclerosis.

Conclusion

Claims 26-32 are rejected. Claims 33-44 are withdrawn as being drawn to a non-elected invention. No claims are allowed

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure are as follows:

a) Edgar et al (US 5880148) which provides a novel combination of fenofibrate and a vitamin E substance.

b) Leibowitz et al (WO 97/28149) provided in the IDS) which describes compounds which are PPARδ agonists. These compounds are useful for rising high

density lipoprotein (HDL) plasma levels in mammals and for preventing, halting or slowing the progression of atherosclerotic cardiovascular diseases.

c) Doebber et al (US 587008) which provides an acetylphenols which are useful as antiobesity an antidiabetic compounds.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 8 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614